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SCIENTIFIC EDITORIAL

Targeting the tricuspid valve: A new therapeutic challenge

La valve tricuspide : un nouveau défi thérapeutique

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Often dysfunctional, difficult to assess with ultrasound techniques, with fewer outcome data and more contradictory results than the other valve diseases, the tricuspid valve (TV) is the most challenging valve for the clinician [1—3]; it is often called the ''forgotten valve''. While TV stenosis is rather uncommon, TV regurgitation (TR) is frequent, but still poorly defined. Trivial TR is frequently detected by echocardiography in normal subjects. Pathological TR is more often secondary, rather than resulting from a primary valve lesion (intrinsic morphopathological changes of the TV complex) [4]. Causes of primary TR are infective endocarditis, rheumatic heart disease, carcinoid syndrome, myxomatous disease, endomyocardial fibrosis, Ebstein's disease, thoracic trauma, pacemaker leads/catheters interfering with leaflet coaptation and drug-induced valve disease. Secondary TR is mainly caused by dilation of the tricuspid annulus and tethering of the TV leaflets secondary to right ventricular dysfunction caused by chronic pressure (i.e. left-sided heart disease or pulmonary hypertension) or volume overload (i.e. atrial septal defects or intrinsic disease of the right ventricle [RV]) [5]. Some authors distinguish a third entity, at the border between primary and secondary TR, so-called ''idiopathic'' TR, in which annular enlargement (possibly of degenerative aetiology, but with normal leaflet morphology) plays the central role in TR genesis [6]. ''Idiopathic''

Abbreviations: 3D, three-dimensional; CMR, cardiac magnetic resonance; CT, computed tomography; RV, right ventricle/ventricular; TR, tricuspid valve regurgitation; TV, tricuspid valve.

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TR is more often observed in elderly patients with atrial fibrillation, but the diagnosis can only be made after exclusion of other potential causes of TR. Distinction between these entities represents the first step in the imaging assessment of TR, as elegantly highlighted in the current issue of the journal by Huttin et al. [7].

Echocardiography is the key imaging method for the evaluation of TR. In fact, the management of patients with TR largely integrates the results of echocardiography; it provides detailed anatomical and functional information, and clarifies the mechanisms that play a role in TR [4]. Presence of vegetations, leaflet thickening and retraction (carcinoid, rheumatic and drug-induced valve disease), prolapsing/flail leaflets (myxomatous or post-traumatic disease) or dysplastic TV with a distance between the tricuspid septal leaflet insertion point to anterior mitral leaflet > 8 mm/m^2 (Ebstein's disease) would plead for primary TR. Secondary TR is confirmed by measurement of the tricuspid annular dimensions, TV deformation, RV function and remodelling, and systolic pulmonary artery pressure. Significant tricuspid annular dilatation is defined by a diastolic diameter $\geq$ 40 mm or $\geq$ 21 mm/m^2 (cut-off derived from surgical studies) in the four-chamber transthoracic view. Significant TV tethering, based on postoperative residual TR after TV repair for secondary TR, is defined as a coaptation distance > 8 mm (distance between the tricuspid annular plane and the point of coaptation in mid-systole from the apical four-chamber view), a tenting area > 1.63 cm^2 and a tethering distance > 0.76 cm. Similar to mitral regurgitation, mixed forms of TR may be encountered in advanced stages of the disease. In these cases, three-dimensional (3D) echocardiography may play a crucial role in outlining the TR aetiology [4].

Colour Doppler echocardiography not only detects the presence of regurgitation, but also permits an understanding of the mechanisms of regurgitation (very eccentric jets may favour primary TR while central jets favour secondary TR) and quantification of its severity and repercussions. Practically, the evaluation of TR requires the use of different echocardiographic modalities (M-mode, Doppler, two-dimensional/3D and transoesophageal echocardiography), should integrate multiple variables and should be supported by clinical data. The width of the vena contracta seems to be the most reliable quantitative index; a vena contracta diameter > 7 mm is a good marker of severe TR. The proximal flow convergence method has been poorly validated, but retained criteria for severe TR affecting patient outcome are an effective regurgitant orifice area > 40 mm^2 and a regurgitant volume > 45 mL [8]. In their review, Huttin et al. emphasized the need to account for respiration-induced changes in TR severity, and the necessity to re-evaluate the patients after optimization of loading conditions, especially when isolated TV surgery is contemplated. The authors also outlined the complementary usefulness of cardiac computed tomography (CT) and cardiac magnetic resonance (CMR) in the assessment of patients with TR [7].

Special attention was also given to the relationship between TR and RV function. The authors reiterated that the RV, being a volume-pump, tolerates an increase in volume overload rather well. Significant TR may thus be clinically silent for a prolonged period, during which progressive RV dilatation and dysfunction may develop [3]. This has led to the general principle that surgery should be carried out early enough to avoid irreversible RV dysfunction [2,3]. However, the load dependency of all echocardiographic and CMR derived variables of RV function, and the fact that some may be altered even in the absence of RV contractile dysfunction, represent non-negligible limitations to the prediction of RV function improvement after corrective surgery [7].

Eventually, the TR patient may be managed with diuretics for symptoms, and only considered for surgery after advanced RV dysfunction, even when liver dysfunction or cirrhosis has developed. It should be no surprise, therefore, that results from the Society of Thoracic Surgeons Database indicated that TV surgery is the most high-risk valve operation in terms of morbidity and mortality [9]. Although mitral valve surgery has evolved over the past few decades towards progressively earlier intervention, even in selected asymptomatic patients, no such evolution has occurred in TV surgery as yet [2,3]. The relative paucity of articles on the TV compared with left-sided valves and the lack of randomized trials have all contributed to intensify this problem. Actually, in patients scheduled for mitral valve surgery, TR is far from uncommon. Historically, TR secondary to mitral valve disease was thought to improve after mitral valve surgery; this led to a conservative non-surgical approach to TR. However, recent studies have clearly challenged this concept, showing excess cardiovascular events when not treated. Therefore, mitral valve surgery alone cannot be expected to result in effective TR control [10].

The current European and American guidelines for the management of valvular heart disease suggest that TV surgery is recommended for patients with severe TR undergoing left-sided valve surgery (Class I), and that TV surgery can be valuable for patients with at least moderate TR with tricuspid annular dilation (Class IIa) [2,3]. Recurrence of TR long after TV plasty is not as uncommon (as high as 60% at 5 years), and surgery may be needed in up to 20% of patients after 10 years [11]. In these patients, as reoperation on the TV carries a very high surgical risk, percutaneous approaches might become valuable alternatives in the near future.

A review of the techniques currently available and a comprehensive description of several cases from experience at Bichat Hospital have been provided in the current issue of the journal by Bouleti et al. [12]. So far, transcatheter interventions for TV disease have been mainly suggested for patients with a degenerating bioprosthesis, with mixed results [13]. Indeed, valve-in-valve reimplantation procedures are subject to fewer complications than valve-in-ring procedures, in which significant paravalvular regurgitation is common in incomplete rigid rings. Valve-in-native valve implantation is more technically challenging. This is the result, in part, of the absence of a rigid landing zone for valve deployment, such as in aortic stenosis, as well as the variety of annular dimensions that may occur in severe TR [14]. This has recently led to some experience with heterotopic placement of transcatheter aortic valves in the inferior vena cava in those patients with refractory peripheral signs of RV failure [15]. Although short-term results are encouraging, long-term studies are needed. Bicuspidization techniques to treat TR are also explained in detail by the

authors. Other newer techniques, such as the FORMA repair system (Edwards Lifesciences, Irvine, CA, USA) and the Millipede system (Millipede, LLC, Ann Arbor, MI, USA) are also reported as means to extend current percutaneous options to TR reduction. The option of transjugular use of the MitraClip system (Abbott Vascular Inc., Santa Clara, CA, USA) to attempt leaflet tethering and decrease functional TR has also been outlined, although such an approach maybe questionable in case of severe tricuspid annulus dilatation and wide malcoaptation gaps.

Currently, there is no single therapeutic approach for the percutaneous treatment of TR, although an increasing number of patients with severe TR exist. General agreement regarding appropriate patient selection, optimal index of treatment and standardized imaging approach (echocardiography, CMR, CT) is necessary for these patients. Clinical and technical challenges associated with percutaneous therapies of TR are preventive features, and represent the next frontiers that clinicians will need to overcome.

Disclosure of interest

The authors declare that they have no competing interest.

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